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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,424	01/26/2004	Stephen J. Karlik	1034008-000061	6792

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
12/19/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/763,424	KARLIK ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-8,10-13,15,16,18-20,22-48 and 52-56* is/are pending in the application.

4a) Of the above claim(s) *25-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-8, 10-13, 15-16, 18-20, 22-24, 46-48 and 52-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/29/08 has been entered.

2. Claims 1-4, 6-8, 10-13, 15-16, 18-20, 22-48 and 52-56 are pending.

3. Claims 25-45 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions.

4. Claims 1-4, 6-8, 10-13, 15-16, 18-20, 22-24, 46-48 and 52-56 are under examination as they read on a method of promoting remyelination of nerve cells or reversing paralysis in a mammal comprising administering a remyelinating agent.

5. The references U and V cited on PTO-892 were provided by Applicant and will not be supplied.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-4, 6-8, 10-13, 15-16, 18-20, 22-24, 46-48 and 52-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of promoting remyelination of nerve cells or reversing paralysis in a multiple sclerosis subject comprising administering to the mammal in need thereof anti-VLA-4 antibody does not reasonably provide **enablement** for "remelination of nerve cells in a mammal", wherein the human suffers from the conditions recited in claim 3, or "reversing paralysis in a subject with a demyelination disease" in claim 46, wherein the subject with paralysis suffers for conditions recited in claim 47. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Action mailed 4/11/06 and 12/21/06.

Applicant's arguments, filed 9/29/08, have been fully considered, but have not been found convincing.

Applicant points to exhibit 1 entitled "Natalizumab Significantly Increases the Cumulative Probability of Sustained Improvement in Physical Disability" Munschauer et al. (setting forth data from the AFFIRM study) demonstrates that not only does the specification enable a method of promoting remyelination, it also demonstrates that the specification enables a method that reverses paralysis in subjects having the conditions recited in claim 47. See in particular Figures 1-4 which present data on the sustained improvement in physical disability in the patients and the "Conclusions" which recites:

> "This analysis provides the first evidence that natalizumab is associated with a significant improvement in functional outcome, rather than only slowing or preventing progression of disability, in a group of patients with relapsing MS." (emphasis added by the Examiner)

This post hoc analysis is of the AFFIRM study population. The methods of the AFFIRM study was published previously in Polman et al. the New England Journal of Medicine (2006) 354(9):899-910 also enclosed. This data illustrates that natalizumab is effective in promoting remyelination and reversing paralysis in demyelinating diseases.

Again, the rejection states that the specification is a method of promoting remyelination of nerve cells or reversing paralysis in a multiple sclerosis subject comprising administering to the mammal in need thereof anti-VLA-4 antibody. However, Applicant did not address the issue at hand as stated in the previous Office Actions, that the "exhibits" fail to show the effect of the natalizumab on a subject with a demyelination disease such as the neuropathies, guillain-barre syndrome a congenital metabolic disorder, a neurophathy with abnormal myelination, drug induced demyelination, radiation induced demyelination, a hereditary demyelinating condition, a prion induced demyelinationg condition, encephalitis induced demyelination, or a spinal cord injury.

Further the AFFIRM study and the Polman et al uses subgenus of MS patient with a baseline EDDS score $\geq$2.0. The abstract teaches that the EDSS score $\geq$2.0 was selected as the cutoff because it reflects a level of disability for patients enrolled in the AFFIRM study that can be measureable improved by effective therapy. Furthermore, the studies uses specific antibodies, Natalizumab, while the claims drawn to generic antibodies.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> *(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.*

9. Claims 1-4, 6-8, 10-13, 15-16, 18-20, 22-24, 46-48 and 52-56 are rejected under 35 U.S.C. 102(a) as being anticipated by National Horizon Scanning Centre article (July 2002).

The article teaches that patients with relapsing-remitting MS (multiple sclerosis) or secondary progressive MS received either IV natalizumab (humanized anti-VLA-4) (3mg/kg or 6mg/kg) or

placebo every 4 weeks for 6 months. MRI results showed that patients treated with natalizumab for 6 months had fewer new brain lesions than those treated wit placebo. A reduction in the number of relapses was also observed, with 34 relapses in the control group compared with 19 in the low dose and 14 in the high dose natalizumab group (see page 3, under Effectiveness). The article teaches that seventy two patients with relapsing-remitting and secondary progressive MS took part in a ranomised double-blind, placebo controlled trial. Each patient received two iv infusions of 3mg/kg natalizumab or placebo four weeks apart and were followed up for 24 weeks with serial MRI and clinical assessment. Significantly fewer new brain lesions were observed in the treated group compared with the control group after first 12 weeks (see page 3, under Effectiveness).

The article teaches that four general methods of disease management target separately or in combination, different aspects of the disease including treatment of relapses with corticosteroids (see page 3, under Current treatment and alternatives).

The reference teachings anticipate the claimed invention.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-4, 6-8, 10-13, 15-16, 18, 46-48 and 52-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tubridy et al (Neurology, 1999 Aug 11;53(3):466-72).

Tubridy et al teaches the effect of anti-α4 integrin antibody on brain lesion activity in MS comprising administering two IV infusions of anti-α4 integrin (3mg/kg) antibody 4 weeks apart and was followed up for 24 weeks with serial MRI and clinical assessment. Tubridy teaches that the treated group exhibited significantly fewer new active lesions and new enhancing lesions than the placebo group over the first 12 weeks. The was no significant difference in the number of new active or new enhancing lesions in the second 12 weeks of the study (see abstract and page 467, under treatment dosage and administration (week 0 and +4)).

Claims 15 and 16 are included because the express dosage amount are material claim limitations however, the statement of the intended result of administering those amounts does not change those amounts or otherwise limit the claim.

While the Tubridy et al article is silence with regard to "remyelination of nerve cells" and "reversing paralysis" per se; the method, the product used in the reference method are the same as the claimed method. Therefore these limitations are considered inherent properties.

The reference teachings does not explicitly teach the chronic administration of anti-VLA-4 is weekly or monthly over a period of at least six moths in claims 1 and 46 or at least one year in claims 18 and 56.

However, Tubridy et al teach their study was not, however, designed to look definitively at the effect of treatment on relapse rate (abstract). Tubridy teach that the relatively modes correlation between disability and changes seen on MRI means that any potential new treatment must ultimately be tested in a larger, longer term trial (see page 471, 2nd col., 1 full ¶). Tubridy et al suggest the use of a higher dose of Antegren (natalizumab) administered chronically will need to be evaluated in future studies (see page 471, 2nd col., 2nd full ¶). Tubridy et al concluded that the treatment was well tolerated. And further studies will be required to determine the longer term effect of this treatment on MRI and clinical out comes (abstract).

However, it would be conventional and within the skill of the art to easily adapt Tubridy et al chronic administration of anti-α4 antibodies to study the longer term and clinical outcome effect of the natalizumab on MS treatment, specially since the natalizumab treatment was well tolerated and show short-term treatment with natalizumab results in a significant reduction in the number of new active lesions on MRI. Further, the Tubridy et al teachings suggest using the chronic administration of natalizumab to study its effect on disability in MS patients.

From the reference teachings, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. Claims 1-4, 6-8, 10-13, 15-16, 18, 46-48 and 52-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 5,840,299 in view of Tubridy et al (Neurology, 1999 Aug 11;53(3):466-72).

The `299 patent teaches a method of treating central nervous system in patient (human) comprising administering to the patient a composition comprising humanized MAB 21.6 (i.e., anti-alpha4beta1 antibody, natalizumab) to block α4-dependent interactions of the VLA-4 receptor (see col., 14, under Methods of Treatment and claims 27-29 in particular). Furthermore, the `299 patent teaches a binding fragment of the humanized antibody. The fragments exhibit

specific binding to the VLA-4 antigen, wherein humanized antibody fragments include separate heavy chains, light chains Fab, Fab', $F(ab')_2$, Fabc, and Fv (see col., 12, under Fragments of Humanized antibodies in particular). In addition, the `299 patent teaches that chimeric light and heavy chains were constructed for the mouse 21.6 $V_L$ and $V_H$ regions (see Example 2, col., 18in particular). The `299 patent also teaches the monoclonal antibody 21.6 (see col., 3, lines 36-39 in particular). The `299 patent teaches that the pharmaceutical compositions can be administered by intravenous or subcutaneous administration. (see col., 15, lines 59-65 in particular). Furthermore, the antibody is administered by intravenous infusion or subcutaneous injection at a dose from 1 to 5 mg antibody per kilo of bodyweight. The dose is repeated at interval from 2 to 8 weeks. Within this range, the preferred treatment regimen is 3 mg antibody per kilo of bodyweight repeated at a 4 week interval (see col., 16, lines 17-22 in particular).

The `299 patent teaches compositions are administered to a patient suspected of, or already suffering from a disease such as multiple sclerosis, in an amount sufficient to cure, or at least partially arrest, the symptoms of the disease and its complications. An amount adequate to accomplish this is defined as a therapeutically- or pharmaceutically-effective dose (see col., 15, lines 41-50). The `299 patent teaches that effective doses of the compositions of the present invention, for the treatment of the above described conditions will vary depending upon many different factors, including means of administration, target site, physiological state of the patient, and other medicants administered (see col., 16, lines 6-18).

Claims 15 and 16 are included because the express dosage amount are material claim limitations however, the statement of the intended result of administering those amounts does not change those amounts or otherwise limit the claim.

While the `299 patent is silence with regard to "remyelination of nerve cells" and "reversing paralysis" per se; the method, the product used in the reference method are the same as the claimed method. Therefore these limitations are considered inherent properties.

The reference teachings does not explicitly teach the chronic administration of anti-VLA-4 is weekly or monthly over a period of at least six moths in claims 1 and 46 or at least one year in claims 18 and 56.

However, Tubridy et al teach that short-term treatment with monoclonal antibody against $\alpha 4$ integrin results in a significant reduction in the number of new active lesions on MRI in MS. Tubridy et al teach that the relatively modest correlation between disability and changes seen on MRI means that any potential new treatment must ultimately be tested in a larger, longer term trial. Finally, Tubridy et al teach that a higher dose of natalizumab administered chronically will need to be evaluated in future studies (see abstract and page 471, 2nd col., 1st and 2nd ¶).

Given that the MS is a chronic disease, and that the `299 patent teachings that administered to a patient suspected of, or already suffering from a disease such as multiple sclerosis, in an amount sufficient to cure, or at least partially arrest, the symptoms of the disease and its complications.

An amount adequate to accomplish this is defined as a therapeutically- or pharmaceutically-effective dose (see col., 15, lines 41-50), it would be conventional and within the skill of the art to chronically administer the anti-VLA-4 as taught by Tubridy et al, weekly or monthly for at least six months/one year. The determination of the optimal intervals of treatment is well within the purview of one of ordinary skill in the art at the time the invention was made and lends no patentable import to the claimed invention. The duration of treatment, the specific rout of administration and like factors within the knowledge and expertise of the medical practitioner. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

As to the administration of the anti-VLA-4 antibodies weekly or monthly over a period of at least six months, such dosing and modes of administration are result effective variables.

It is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also Merck & Co. v. Biocraft Labs. Inc., 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious).

As dosing and modes of administration are known to the ordinary artisan, it would have been obvious to optimize both the dosing regimens and mode of administration to meet the needs of the patient at the time the invention was made.

Given the clear teachings of the prior art to treat MS with humanized MAB 21.6 antibodies to block α4-dependent interactions of the VLA-4 receptor including in therapeutic regimens for treating disease such as multiple sclerosis, in an amount sufficient to cure, or at least partially arrest, the symptoms of the disease and its complications; one of ordinary skill in the art at the time the invention was made would have been motivated to administer various therapeutic regimens including the treatment of MS with anti-VLA-4 antibodies weekly or monthly over a period of at least six months, at the time the invention was made.

The various dosing regimens encompassed by the instant claims were obvious at the time the invention was made, given that it was well known and practice at the time the invention was made to provide immunotherapy based upon the condition and needs of the patient, as evidenced by the teachings of the prior art.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdiqital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

13. Claims 1-4, 19-20 and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 5,840,299, in view of Tubridy et al, and further in view of U.S. Pat. No 6,753,135 as set forth in the previous Office Action mailed 4/11/06.

Applicant's arguments, filed 9/29/08, have been fully considered, but have not been found convincing.

Applicant submits that their teachings for chronic administration of natalizumab has displayed unexpected benefits in the treatment of demyelinating conditions. Applicant points to Munschauer et al poster exhibit demonstrates that the chronic administration of natalizumab over time not only promotes remyelination, but it reverses paralysis in subjects. None of the cited references disclose these benefits of chronic administration. Thus, not only do the cited references fail to disclose chronic administration of anti-VLA-4 antibodies, but the references fail to disclose the reduction of demyelination caused by demyelinating disease states. Accordingly, at the time invention was made one of ordinary skill in the art would not have had an expectation of successfully achieving the effect of reduction of demyelination, and accordingly would not have combined the elements of the cited references to arrive at the present invention. Furthermore, there is no motivation to combine the secondary references cited by the Office with U.S. Patent No. 5,840,299 and even if combined, the combination fails to resolve the differences between the primary references, the '299 patent, and the claims in issue.

However, the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. In re Linter, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972) (discussed below); In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990), cert. denied, 500 U.S. 904 (1991)

(discussed below). Although Ex parte Levengood, 28 USPQ2d 1300, 1302 (Bd. Pat. App. & Inter. 1993) states that obviousness cannot be established by combining references "without also providing evidence of the motivating force which would impel one skilled in the art to do what the patent applicant has done " (emphasis added), reading the quotation in context it is clear that while there must be motivation to make the claimed invention, there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention.

As to the administration of the anti-VLA-4 antibodies weekly or monthly over a period of at least six months, such dosing and modes of administration are result effective variables.

It is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also Merck & Co. v. Biocraft Labs. Inc., 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious).

As dosing and modes of administration are known to the ordinary artisan, it would have been obvious to optimize both the dosing regimens and mode of administration to meet the needs of the patient at the time the invention was made.

Given the clear teachings of the prior art to treat MS with humanized MAB 21.6 antibodies to block α4-dependent interactions of the VLA-4 receptor including in therapeutic regimens for treating disease such as multiple sclerosis, in an amount sufficient to cure, or at least partially arrest, the symptoms of the disease and its complications; one of ordinary skill in the art at the time the invention was made would have been motivated to administer various therapeutic regimens including the treatment of MS with anti-VLA-4 antibodies weekly or monthly over a period of at least six months, at the time the invention was made.

The various dosing regimens encompassed by the instant claims were obvious at the time the invention was made, given that it was well known and practice at the time the invention was made to provide immunotherapy based upon the condition and needs of the patient, as evidenced by the teachings of the prior art. Chronic disease such as MS requires maintenance drug. Thus the skilled in the art would be motivated to administer the anti-VLA-4 antibodies weekly or monthly over a period of at least six months to treat a chronic MS disease.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B. O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

December 15, 2008

/Maher M. Haddad/
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